9200/1643

PATENT
600-1-266N

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT :	Kreek, M.J. *et al.*		
SERIAL NO. :	09/883,839	EXAMINER :	Unknown
FILED :	June 18, 2001	ART UNIT :	1643
FOR :	ALLELES OF THE HUMAN MU OPIOID RECEPTOR, DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS OF TREATMENT BASED THEREON		

CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to MAIL STOP AF, COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 on April 5, 2004.

Betty Schultz
(Name of Depositor)

Betty Schultz 4/5/04
(Signature and Date)

REQUEST FOR WITHDRAWAL OF INCORRECT ABANDONMENT

MAIL STOP AF
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA , VA 22313-1450

Dear Sir:

Applicants request herewith that the Notice of Abandonment dated November 18, 2003 be vacated, as a proper response to the Notice to File Missing Parts dated July 20, 2001 was filed.

In the present instance, a Request for a One-Month Time Extension was submitted together with a Preliminary Amendment, an executed Declaration and Power of Attorney, a transmittal sheet, a PTOSB17 form, and a check in the amount of $1,317.00. All items were effectively mailed on October 15, 2001. In support of Applicant's entitlement for withdrawal of the Notice of Abandonment, Applicant submits herewith copies of the One-Month Time Extension, the executed Declaration and Power of Attorney, the Preliminary Amendment, the transmittal sheet, the PTOSB17 form, and the corresponding canceled postcard receipts with respect to each.

Furthermore, Applicants' Representative respectfully notes that the second page of the

Notice to File Missing Parts was not included in the original notice as received by Applicant. Please forward the missing page such that Applicants can respond to any deficiencies that may be outstanding.

Favorable consideration and withdrawal of the Notice of Abandonment, and restoration of the present application to the pending roles for purposes of further processing, are believed to be in order, and are courteously solicited.

Respectfully submitted,

Veronica Mallon

VERONICA MALLON, Ph.D.
Agent for Applicant(s)
Registration No. 52,491

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, NJ 07601
(201) 487-5800
Enclosures

Date: April 5, 2004

Serial No. 09/883,839 File No. 600-1-266N By DAJ/MAY/aj

Title ALLELES OF THE HUMAN MU OPOID RECEPTOR, ...

In the Matter of the Application of Mary Jeanne Kreek et al.

The following was received in the U.S. Patent & Trademark Office on the date stamped hereon: via first-class mail

- ☒ Transmittal Sheet/Cover Ltr.
- ☐ Application For Patent
- Executed ☒ Declaration ☐ Affidavit
- ☐ Drawings ☐ Sheet(s)
- ☐ S.E. Verified Statements
- ☐ Assignment
- ☒ Check for $ 1,317.00
- ☐ Letter ☒ Missing Parts
- ☐ Priority Document
- ☒ Amendment ☐ Response
  Preliminary
- ☒ Extension of Time 1 Month
- ☐ Issue Fee Transmittal
- ☐ Maintenance Fee
- ☐ Appln. TM Registration
- ☐ 8 & 15 Declaration
- ☐ Renewal Application
- ☐ Notice of Appeal
- ☐ Brief ☐ Petition
- ☐ Power of Attorney
- ☒ PTOSB17

Serial No. 09/883,839 File No. 600-1-266N By DAJ/MAY/aj

Title ALLELES OF THE HUMAN MU OPOID RECEPTOR, ...

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The following was received in the U.S. Patent & Trademark Office on the date stamped hereon: via first-class mail

Executed

- [X] Transmittal Sheet/Cover Ltr.
- [ ] Application For Patent
- [X] Declaration [ ] Affidavit
- [ ] Drawings [ ] Sheet(s)
- [ ] S.E. Verified Statements
- [ ] Assignment
- [X] Check for $ 1,317.00
- [ ] Letter [X] Missing Parts
- [ ] Priority Document
- [X] Amendment [ ] Response Preliminary
- [X] Extension of Time 1 Month
- [ ] Issue Fee Transmittal
- [ ] Maintenance Fee
- [ ] Appln. TM Registration
- [ ] 8 & 15 Declaration
- [ ] Renewal Application
- [ ] Notice of Appeal
- [ ] Brief [ ] Petition
- [ ] Power of Attorney
- [X] PTOSB17

Security enhanced document See back for details

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HACKENSACK, NJ 07601

SUMMIT BANK 401 Hackensack Ave. Hackensack, N.J. 07601

13135

55-216/212
11

DATE 10/15/01

PAY TO THE ORDER OF COMMISSIONER OF PATENTS AND TRADEMARKS $ 1317.00

One Thousand three hundred seventeen & 00/100 DOLLARS

THIS CHECK IS DELIVERED IN CONNECTION WITH THE FOLLOWING ACCOUNTS

600-1-266N			
09/883,839			
MP			

Joann Rodgers MP

⑈013135⑈ ⑆021202162⑆ 134⑈00688 7⑈

mailed 10/15/01

Please type a plus sign (+) inside this box → [+]

PTO/SB/21 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/883,839
Filing Date	June 18, 2001
First Named Inventor	Mary Jeanne Kreek et al
Group Art Unit	1643
Examiner Name	TBA
Total Number of Pages in This Submission	
Attorney Docket Number	600-1-266N

ENCLOSURES *(check all that apply)*

- [X] Fee Transmittal Form
  - [X] Fee Attached
- [X] Amendment / Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [X] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [X] Response to Missing Parts/ Incomplete Application
  - [X] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group (*Appeal Notice, Brief, Reply Brief*)
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) *(please identify below)*: Executed Declaration, Postcard & Check

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	David A. Jackson, Reg. No. 26,742
Signature	
Date	10/15/2001

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: October 15, 2001

Typed or printed name	Anne M. Jones		
Signature		Date	October 15, 2001

PTO/SB/17 (11-00)
Approved for use through 10/31/2002. OMB 0651-0032
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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

FEE TRANSMITTAL for FY 2001

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT ($)1,317.00

Complete if Known	
Application Number	09/883,839
Filing Date	June 18, 2001
First Named Inventor	Mary Jeanne Kreek et al.
Examiner Name	TBA
Group Art Unit	1643
Attorney Docket No.	600-1-266N

METHOD OF PAYMENT

1. [X] The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number: 11-1153

Deposit Account Name:

[X] Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17

[X] Applicant claims small entity status. See 37 CFR 1.27

2. [X] **Payment Enclosed:**

[X] Check [ ] Credit card [ ] Money Order [ ] Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	710	201	355	Utility filing fee	370.00
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	

SUBTOTAL (1) ($) 370.00

2. EXTRA CLAIM FEES

			Extra Claims		Fee from below	Fee Paid
Total Claims	59	-20** =	39	X	9.00	=351.00
Independent Claims	11	- 3** =	8	X	42.00	=336.00
Multiple Dependent					140.	=140.00

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 827.00

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	65.00
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	55.00
116	390	216	195	Extension for reply within second month	
117	890	217	445	Extension for reply within third month	
118	1,390	218	695	Extension for reply within fourth month	
128	1,890	228	945	Extension for reply within fifth month	
119	310	219	155	Notice of Appeal	
120	310	220	155	Filing a brief in support of an appeal	
121	270	221	135	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,240	241	620	Petition to revive - unintentional	
142	1,240	242	620	Utility issue fee (or reissue)	
143	440	243	220	Design issue fee	
144	600	244	300	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	710	246	355	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249	355	For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279	355	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 120.00

SUBMITTED BY				Complete (if applicable)	
Name (Print/Type)	David A. Jackson	Registration No. (Attorney/Agent)	26,742	Telephone	201-487-5800
Signature				Date	October 15, 2001

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231: DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

600-1-266 N

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: MARY JEANNE KREEK et al.

SERIAL NO.: 09/883,839 EXAMINER: Unknown

FILED: June 18, 2001 ART UNIT: 1643

FOR: ALLELES OF THE HUMAN MU OPIOID RECEPTOR, DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS OF TREATMENT BASED THEREON

Certificate of Mailing Under 37 CFR 1.8

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David A. Jackson, Reg. No. 26,742
(Name of Registered Rep.)

(Signature and Date) 10/15/01

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, DC 20231

Dear Sir:

Prior to calculating claim fees, please enter the following amendments into the file of the present application.

IN THE CLAIMS:

Please cancel claims 1-83 without prejudice or disclaimer and add the following new claims 84-141.

84. A variant allele of a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof.

85. The variant allele of claim 84 wherein said variant allele is isolated.

86. The isolated variant allele of Claim 85, detectably labeled.

87. An isolated nucleic acid molecule selectively hybridizable to the isolated variant allele of Claim 85.

88. The isolated nucleic acid molecule of Claim 87, detectably labeled.

89. A variant allele of a human mu opioid receptor gene which encodes a variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.

90. The variant allele of claim 89 wherein said variant allele is isolated.

91. A isolated variant human mu opioid receptor comprising an amino acid sequence having a variation in SEQ ID NO:2, wherein said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63.

92. An antibody having a variant human mu opioid receptor of Claim 91 as an immunogen.

93. The antibody of Claim 92, detectably labeled

94. A cloning or expression vector comprising an isolated variant allele of a human mu opioid

receptor gene and an origin of replication, wherein said variant allele comprises a DNA of claim 84.

95. A cloning or expression vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84.

96. An expression vector comprising an isolated variant allele of a human mu opioid receptor gene comprising a DNA sequence of claim 84.

97. An expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence of claim 84.

98. A unicellular host transformed or transfected with an expression vector comprising an isolated variant allele of a human mu opioid receptor gene operatively associated with a promoter, wherein said variant allele comprises a DNA sequence of claim 84.

99. A unicellular host transformed with an expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence of claim 84.

100. An isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein said variations comprise T67C; T124A; C153T; G174A or 187INS:GGC.

101. The isolated variant allele of Claim 100 detectably labeled.

102. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene comprising a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1.

103. The isolated nucleic acid molecule of Claim 102, detectably labeled.

104. An isolated variant allele of a human mu opioid receptor gene, which encodes a variant human mu opioid receptor comprising an amino acid sequence having at least two variations in SEQ ID NO:2, wherein at least one said variation comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.

105. An isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene of claim 84, wherein and said variant allele comprises a DNA sequence having at least two variations in SEQ ID NO:1, and at least one of said variations comprises T67C; T124A; C153T; G174A or 187INS:GGC, so that said isolated nucleic acid molecule encodes a variant human mu opioid receptor comprising at least two variations in sequence of SEQ ID NO:2, wherein at least one of said variations comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.

106. A variant human mu opioid receptor of claim 91 comprising an amino acid sequence having at least two variations in SEQ ID NO:2, wherein at least one of said variations comprises Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly63.

107. An antibody having a variant human mu opioid receptor of Claim 106 as an immunogen.

108. The antibody of Claim 107, detectably labeled.

109. A cloning or expression vector comprising an isolated variant allele of a human mu opioid receptor gene and an origin of replication, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein at least one of said variations comprises T67C; T124A; C153T; G174A; or 187INS:GGC.

110. A cloning or expression vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human mu opioid receptor gene, wherein said variant allele comprises a DNA sequence of claim 84 having at least two variations in SEQ ID NO:1, wherein at least one of said variations comprises T67C; T124A; C153T; G174A; or 187INS:GGC.

111. A unicellular host transformed with an expression vector of Claim 109.

112. A unicellular host transformed with an expression vector of Claim 110.

113. A method for determining a susceptibility in a subject to at least one addictive disease,

comprising the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;

b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence of claim 84,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to at least one addictive disease relative to the susceptibility to said at least one addictive disease in a standard.

114. The method for determining a susceptibility to at least one addictive disease of Claim 113, further comprising the step of determining whether said human mu opioid receptor gene of said second allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said human mu opioid receptor gene of said second allele is expected to be indicative of the subject's susceptibility to said at least one addictive disease relative to the susceptibility to said at least one addictive disease in said standard.

115. The method of either of Claim 114 wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.

116. A method for determining a susceptibility to at least one addictive disease in a subject relative to susceptibility in a standard, comprising the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a human mu

opioid receptor;

b) determining whether said human mu opioid receptor comprises an amino acid sequence of claim 91,

such that the presence of said at least one variation is expected to be indicative of the susceptibility to said at least one addictive disease in said subject relative to susceptibility to said at least one addictive disease in said standard, wherein the human mu opioid receptor of said standard comprises an amino acid sequence of SEQ ID NO:2.

117. The method of Claim 116, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.

118. A method for determining a susceptibility to pain in a subject relative to a susceptibility of pain in a standard, wherein the method comprises the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;

b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence of claim 84,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

119. The method of Claim 118 for determining a susceptibility to pain in a subject, further comprising

the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility of pain in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

120. A method for determining a therapeutically effective amount of pain reliever to administer to a subject in order to induce analgesia in said subject relative to a therapeutically effective amount of pain reliever to administer to a standard in order to induce analgesia in said standard, wherein the method comprises determining a susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein susceptibility to pain in said subject is expected to be indicative of said therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject relative to said therapeutically effective amount of pain reliever to administer to said standard to induce analgesia in said standard.

121. The method of Claim 120 for determining a therapeutically effective amount of pain reliever to administer to said subject, wherein determining susceptibility to pain in said subject comprises the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and

b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation

comprises T67C; T124A; C153T; G174A or 187INS:GGC, or combinations thereof, wherein the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the subject's susceptibility to pain relative to said to susceptibility of pain in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, such that said therapeutically effective amount of pain reliever to administer to the subject in order to induce analgesia is related to said susceptibility to pain in said subject relative to susceptibility to pain in said standard.

122. The method of Claim 121, wherein determining susceptibility to pain in said subject relative to susceptibility to pain in said standard further comprises the step of determining whether said second allele of said bodily sample from said subject comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises T67C, T124A or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1, and the therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject is related to the presence of said at least one variation in said human mu opioid receptor gene of said second allele of said bodily sample from said subject.

123. A method for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from at least one addictive disease to treat the at least one addictive disease in said subject relative to a therapeutically effective amount of therapeutic agent to administer to

a standard suffering from the at least one addictive disease to treat the at least one addictive disease in said standard, wherein the method comprises the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and

b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C, T124A or 187INS:GGC,

wherein the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of the therapeutically effective amount of said therapeutic agent to administer to the subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

124. The method of Claim 123 for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from said at least one addictive disease to treat said at least one addictive disease, relative to said therapeutically effective amount of said therapeutic agent administered to said standard suffering from said at least one addictive disease to treat said at least one addictive disease in said standard, further comprising the step of determining whether said second allele of said bodily sample from said subject comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele related to said therapeutically effective amount of said therapeutic

agent administered to said subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

125. The method of either of Claims 123 or 124, wherein said at least one addictive disease comprises opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine addiction; barbiturate or sedative hypnotic addiction; anxiolytic addiction; or alcohol addiction.

126. A commercial test kit may for determining the presence of at least one variation in a human mu opioid receptor gene of an allele in a bodily sample taken from a subject, wherein the commercial test kit comprises:

a) PCR oligonucleotide primers suitable for detection of an allele comprising a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1 comprising T67C; T124A; C153T; G174A; or 187INS:GGC;

b) other reagents; and

c) directions for use of the kit.

127. A commercial test kit for detecting a variant human mu opioid receptor in a bodily sample taken from a subject, comprising

(a) predetermined amount of at least one detectably labeled immunochemically reactive component having affinity for a variant human mu opioid receptor; said variant being at least one of Ser23Pro, Ser42Thr or the addition of a Gly residue following Gly 63;

(b) other reagents; and

(c) directions for use of the kit.

128. A commercial test kit for detecting a variant human mu opioid receptor in a bodily sample taken from a subject, wherein said kit comprises:

(a) a labeled component which has been obtained by coupling the human mu opioid receptor of the bodily sample to a detectable label;

(b) one or more additional immunochemical reagents of which at least one reagent is a ligand or an immobilized ligand, which ligand comprises:

(i) a ligand capable of binding with the labeled component (a);

(ii) a ligand capable of binding with a binding partner of the labeled component (a);

(iii) a ligand capable of binding with at least one of the component(s) to be determined; or

(iv) a ligand capable of binding with at least one of the binding partners of at least one of the component(s) to be determined;

(c) directions for the performance of a protocol for the detection and/or determination of one or more components of an immunochemical reaction between the human mu opioid receptor and a specific binding partner thereto.

129. A method for diagnosing a disease or disorder related to a physiological function regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus pituitary gonadal axis (HPG), wherein the method comprises the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene;

b) determining whether said human mu opioid receptor gene of said first allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC,

such that the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the hypothalamus pituitary adrenal axis (HPA) or the hypothalamus pituitary gonadal axis (HPG), wherein said first allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

130. The method of Claim 129, wherein said physiological function comprises sexual or reproductive function, gastrointestinal motility, immune response, or ability to withstand stress.

131. The method of Claim 130, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to said standard, or decreased ability to withstand stress relative to said standard.

132. The method of Claim 130 for diagnosing a disease or disorder related to a physiological function regulated by the HPA or HPG, further comprising the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

133. The method of Claim 132, wherein said physiological function comprises sexual or reproductive function, gastrointestinal motility, immune response, or ability to withstand stress.

134. The method of Claim 132, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to said standard, or decreased ability to withstand stress relative to said standard.

135. The method of Claim 132, wherein said disease or disorder comprises diarrhea.

136. A method for selecting an appropriate therapeutic agent and a therapeutically effective amount of said agent to administer to said subject to treating a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein the method comprises diagnosing said disease or disorder in said subject, wherein said disease or disorder is expected to be indicative of said appropriate therapeutic agent for treating said disease or disorder.

137. The method of Claim 136, wherein said physiological function comprises reproductive or sexual function, gastrointestinal motility, immune response, or ability to withstand stress.

138. The method of Claim 136, wherein diagnosing said disease or disorder in said subject comprises the steps of:

a) removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human mu opioid receptor gene; and

b) determining whether said first allele comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said

at least one variation comprises T67C; T124A; or 187INS:GGC,

wherein the presence of said at least one variation in said human mu opioid receptor gene of said first allele is expected to be indicative of said disease or disorder related to a physiological function regulated by the HPA or HPG axes.

139. The method of Claim 138, wherein diagnosing a disease or disorder related to a physiological function regulated by the HPA or HPG further comprises the step of determining whether said second allele of said bodily sample comprises a human mu opioid receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises T67C; T124A; or 187INS:GGC, such that the presence of said at least one variation in said second allele is expected to be indicative of a disease or disorder related to a physiological function regulated by the HPA or HPG axes, wherein said second allele of said standard comprises a human mu opioid receptor gene comprising a DNA sequence of SEQ ID NO:1.

140. The method of Claim 139, wherein said physiological function comprises reproductive or sexual function, gastrointestinal motility, immune response, or ability to withstand stress.

141. The method of Claim 139, wherein said disease or disorder comprises infertility, constipation, diarrhea, decreased immune response relative to immune response in said standard, or decreased ability to withstand stress relative to ability to withstand stress of said standard.

Remarks

The new claims presented above which replace the original claims contain no new matter

and were provided simply to reduce the number of claims in the application. Examination on the merits is courteously solicited.

Respectfully submitted,

KLAUBER & JACKSON

David A. Jackson
Attorney for Applicants
Reg. No. 26,742

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PATENT
600-1-266 N

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: MARY JEANNE KREEK *ET AL.*

SERIAL NO.: 09/883,839 EXAMINER: UNASSIGNED

FILED: June 18, 2001 ART UNIT: 1643

FOR: ALLELES OF THE HUMAN MU OPIOID RECEPTOR, DIAGNOSTIC METHODS USING SAID ALLELES, AND METHODS OF TREATMENT BASED THEREON

Certificate of Mailing Under 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 on October 15, 2001.

David A. Jackson, Reg. No. 26,742
(Name of Registered Rep.)

(Signature and Date)

PETITION FOR ONE-MONTH EXTENSION OF TIME

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Dear Sir:

Applicants hereby request that the period for responding to the Notice to File Missing Parts of Non-Provisional Application now set to expire on September 20, 2001, be extended by one (1) month, so as to expire on October 20, 2001.

As Applicants are associated with a small entity, a check in the amount of $1,317.00 is enclosed to cover the fees involved in filing the One-Month Extension and Missing Parts of the Application. The Commissioner is further authorized to charge any deficiencies or to credit any overages to Deposit Account No. 11-1153.

PATENT
600-1-266 N

Favorable action on this Request for Extension of Time is courteously solicited.

Respectfully submitted,

David A. Jackson
Attorney for Applicant(s)
Registration No. 26,742

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, NJ 07601
(201) 487-5800

Date:

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
WASHINGTON, D.C. 20231
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
09/883,839	06/18/2001	Mary Jeanne Kreek	600-1-266 N

CONFIRMATION NO. 9969

FORMALITIES LETTER

OC000000006321355

23565
KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

Date Mailed: 07/20/2001

Due 9/20/01
OOD 1/20/02

NOTICE TO FILE MISSING PARTS OF NONPROVISIONAL APPLICATION

FILED UNDER 37 CFR 1.53(b)

Filing Date Granted

An application number and filing date have been accorded to this application. The item(s) indicated below, however, are missing. Applicant is given **TWO MONTHS** from the date of this Notice within which to file all required items and pay any fees required below to avoid abandonment. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

- The statutory basic filing fee is missing.
  Applicant must submit $ **355** *to complete the basic filing fee and/or file a small entity statement claiming such status (37 CFR 1.27).*
- Total additional claim fee(s) for this application is $1872.
  - **$657** for **73** total claims over 20.
  - **$1080** for **27** independent claims over 3 .
  - **$135** for multiple dependent claim surcharge.
- The oath or declaration is unsigned.
- To avoid abandonment, a late filing fee or oath or declaration surcharge as set forth in 37 CFR 1.16(e) of $65 for a small entity in compliance with 37 CFR 1.27, must be submitted with the missing items identified in this letter.
- **The balance due by applicant is $ 2292.**

The application is informal since it does not comply with the regulations for the reason(s) indicated below.

The required item(s) identified below must be timely submitted to avoid abandonment:

- Substitute drawings in compliance with 37 CFR 1.84 because:
  - drawing sheets do not have the appropriate margin(s) (see 37 CFR 1.84(g)). Each sheet must include a top margin of at least 2.5 cm. (1 inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 1.5 cm. (5/8 inch), and a bottom margin of at least 1.0 cm. (3/8 inch);
- This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May